

## $\alpha$ 1-Antitrypsin

### 00719. $\alpha$ <sub>1</sub>-Antitrypsin

#### Explanatory Notes

[9041-92-3]  $\alpha$ <sub>1</sub>-Trypsin inhibitor;  $\alpha$ <sub>1</sub>-proteinase inhibitor;  $\alpha$ <sub>1</sub>-protease inhibitor;  $\alpha$ <sub>1</sub>-antitrypsin; AAT; A1AT; A1PI. Aralast (Baxter); Prolastin (Bayer); Zemaira (ZLB Behring). Serum glycoprotein synthesized by the liver. Major serine protease inhibitor (serpin) in mammalian plasma; primarily inhibits neutrophil elastase. Consists of a single polypeptide chain of 394 amino acid residues and 3 carbohydrate side chains linked to asparagine residues. Mol wt ~52,000 daltons. Highly pleomorphic protein with a number of genetic variants. Characterization of trypsin inhibitor in  $\alpha$ <sub>1</sub>-fraction of human serum: K. Jacobsson, *Scand. J. Clin. Invest.* **7**, Suppl. 14, 57-102 (1955). Isoln from human serum: F. C. Moll *et al.*, *J. Biol. Chem.* **233**, 121 (1958); H. F. Bundy, J. W. Mehl, *ibid.* **234**, 1124 (1959). Purification: I. P. Crawford, *Arch. Biochem. Biophys.* **156**, 215 (1973); M. H. Coan, W. J. Brockway, **US 4379087** (1983 to Cutter). Structural study of active site: D. Johnson, J. Travis, *J. Biol. Chem.* **253**, 7142 (1978). Complete amino acid sequence and review of genetic variants: R. W. Carrell *et al.*, *Nature* **298**, 329 (1982). Crystal structure: H. Loebermann *et al.*, *J. Mol. Biol.* **177**, 531 (1984). Cloning and expression of human AAT gene: M. Courtney *et al.*, *Proc. Natl. Acad. Sci. USA* **81**, 669 (1984). AAT deficiency has been associated with degenerative lung disease: C.-B. Laurell, S. Eriksson, *Scand. J. Clin. Lab. Invest.* **15**, 132 (1963); with hepatic cirrhosis: H. L. Sharp, *Gastroenterology* **70**, 611 (1976). Inhibition of leukocyte elastase: K. Ohlsson, *Scand. J. Clin. Lab. Invest.* **28**, 251 (1971); K. Beatty *et al.*, *J. Biol. Chem.* **255**, 3931 (1980). Review of human phenotypes and relationship to disease: J. O. Morse, *N. Engl. J. Med.* **299**, 1045-1048; 1099-1105 (1978). Clinical evaluation in AAT deficiency: M. D. Werwers *et al.*, *ibid.* **316**, 1055 (1987); N. Konietzko *et al.*, *Dtsch. Med. Wochenschr.* **113**, 369 (1988); of the effect of cigarette smoking on the association rate constant with neutrophil elastase: F. Ogushi *et al.*, *J. Clin. Invest.* **87**, 1060 (1991). Symposium on structure, function and clinical applications: *Am. J. Med.* **84**, Suppl. 6A, 1-90 (1988). Review of role in emphysema: P. J. Stone, *Clin. Chest Med.* **4**, 405-412 (1983); J. A. Pierce, *J. Am. Med. Assoc.* **259**, 2890-2895 (1988).

THERAP CAT: In treatment of emphysema associated with inherited  $\alpha$ <sub>1</sub>-antitrypsin deficiency.

KEYWORD(S): Enzyme Replacement Therapy.